INTERVIEW WITH

Dr. BRUCE GELLIN

H1N1 ORAL HISTORY PROJECT

Interviewed By Sheena Morrison

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Interview with Dr. Bruce Gellin
Interviewed at Dr. Gellin's Office,
Washington D.C., U.S.A.
Interviewed on November 13th, 2009
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Dr. Bruce Gellin: BG
Sheena Morrison: SM

SM: The following interview was conducted with Dr. Bruce Gellin, Director of the National Vaccine Program within the Department of Health and Human Services. It was conducted on behalf of the National Library of Medicine for the Making History: H1N1 Oral History Project. It took place on November 13th at Dr. Gellin's office in Washington, DC. The interviewer is Sheena Morrison.

So the first question will be a little bit about yourself. How long have you been in your current position as Director of the National Vaccine Program?

BG: I came here in October of 2002, and at the time the National Vaccine Program office was in transition. It's history had been that it was started in the late '80's as part of the legislation that brought in the National Vaccine Injury Compensation Program. The recognition at

that time was about vaccine supply, and there was concerns about disruptions in supply if manufacturers started leaving the vaccine business, in part, because of lawsuits about vaccine side effects. So that's the history of the program. It had been here since in the mid '90's in Washington within the Assistant Secretary for Health's office, and then it went to CDC in the mid '90's, and it was there for several years until the person who was then the director decided to move on to something else. The position was open, and that gave the department an opportunity to revisit how they wanted it to sit organizationally. So, I came here in October 2002, and my sense was that that was a time then - after 9/11, after the anthrax attacks - when the H5N1 virus was just beginning to resurface in Asia after having an episode in the late '90's, particularly in Hong Kong. And it was right before SARS emerged. So, I think it was in all that setting and the recognition that that the country didn't have a pandemic preparedness plan.

So, because historically the National Vaccine Program office was a place for interagency scientific discussion and collaboration, pandemic preparedness and pandemic planning was organizationally housed here. And then there

had been some discussions prior to my being here about pandemic planning, but it was seemingly much more of an academic exercise. When there was much more concern about having real preparedness to mount a real response is when there was insistence, at that point, by Secretary Thompson that we have such a plan. And that was my first, second and third priority when I got here.

SM: Now can you explain to me your role in the Federal Government's planning and response efforts to the 2009 H1N1 outbreak.

BG: Well, then again, I'll back up to how this all started. They wanted to have a central place within the Secretary's office where pandemic preparedness – again, in general pandemic preparedness, not H1N1 - would go on. That's how I and this office became involved in this. But obviously, this is a small office, and it was just an organizing principle to reach into the other parts of the department, particularly CDC, NIH and FDA, but more broadly about pandemic preparedness.

In 2004 we wrote the first draft of a pandemic plan that we put out as a draft for public comment. And I remember we

put it out in August, and our intention for doing it in August was to keep it away from the seasonal flu season so it wouldn't, so people wouldn't be confused by it. I should look back because the day we put it out, there were two other articles that came out: one about antiviral resistance, and something else.

And so, all of a sudden you found yourselves talking about pandemic preparedness in August, and we're readily in the news in the summer about influenza. We put out that draft plan for public comment and got relatively few. My recollection is maybe about 50 people commented. It was posted on the website for four or six weeks. Most of the people who responded were the usual people you'd expect to respond: the people who have a vested interest in influenza primarily, but I think it tells you about the level of interest in pandemic preparedness circa 2004 versus what it then became. We took those comments seriously. We had a number of internal discussions, and then developed what was then the HHS plan that was released in November 2005.

As we were developing that plan, (again, this was the HHS plan,) because we realized that while the National Vaccine Program office was a reasonable place for this activity to

sit, pandemic preparedness was much more than just the vaccine part. That was in a simple way what people thought of, but as you got more and more into it realized that a vaccine was just one of many, many elements of just a health response. In a severe pandemic, it was much to this than health alone. As we had discussions, not only across HHS, but with other departments and at that point the Homeland Security Council at the White House, it became very apparent that the plan we were working on was really the public health and health response to a pandemic, and not the Government's broad response. So with that, as we were moving to release our plan, we felt that it was important to have that so that states and locals and health systems could begin making their own planning to have some insights as to what the Federal Government was thinking about.

That's when Homeland Security Council recognized that there was more to this than the health component. And in the process of our finalizing our plan, they developed what was called a 'national strategy for pandemic influenza preparedness' (I forget the exact name). So that became essentially the umbrella document that gave the architectural framework for the broad pandemic response by

the U.S. Government. Again, it was a broad high level strategic plan for which the other plans like ours from HHS would fit underneath it. So theirs ultimately was released November 1st, 2005, at a time when President Bush went to the National Institutes of Health to talk about pandemic preparedness, and the recognition that it was gonna require additional resources to bring us up to a level of preparedness far beyond what we were now.

So, at that session on November 1st, at the Natcher Center at NIH, he then announced that the White House's plan - he previewed in a way the HHS plan, but more importantly signaled the need for huge expenditures to bring up our preparedness - and at that point asked for $7.1 Billion to do a whole range of things. The largest piece of that was on improving the vaccine infrastructure to be able to mount a response with vaccine, but again much more than just the vaccine piece.

But I didn't answer your question. So now, that was 2005. The focus then was on the H5N1 virus, the bird flu virus, which by the way hasn't gone away. And I think there are a lot of concerns about the potential that virus has to trigger a pandemic. And again, highlighting that these

influenza viruses can always emerge and trigger a pandemic, what was especially concerning about, and continues to be concerning, about the H5N1 virus is it's very high fatality rate. We are fortunate that it has not developed the ability to transmit among people. We know that there is broad population susceptibility to this, but it doesn't have that other characteristic of sustained person to person transmission. There is always the concern that it could unlock the code and develop the mutation that would allow that to happen, and it's still a concern. And every time there are cases, particularly when there are small clusters of H5N1, is the question of whether or not the virus has changed to allow some of that - with a fatality rate at about 2/3 that may be higher than any other infectious disease, which is why there was so much concern about the bird flu virus.

And then, all of the discussions about the virus, circa 1918. So, if you recall that in 1918 the global pandemic had a case fatality rate of about 2%, that's why the H5N1's virus fatality rate of 60+% was of such concern. So that's what generated a lot of our interest in this sense of urgency of never knowing if this virus would flip and

become the pandemic virus with all the pandemic potential; I think that accelerated all of our concerns about that.

SM: And so, as a result it became a primary responsibility to be prepared for any new virus or the potential for H5N1 to go pandemic?

BG: I think in the recent setting of SARS, which there are, it's a good example and not such a good example of what might happen. But that just shows in our current society and economy and the way that society is strung together, how quickly viruses can get around the world. In World War I, I think it was largely from the movement of troops in World War I, and now you can be anywhere in the world within 24 hours. And I think the experience of SARS and how rapidly that could find its place to other locales was a signal for how severe and how quickly this could take off.

So, again, the focus has been primarily around influenza and building on a number of influenza specific systems. At the same time, recognizing that this response was not H5N1, and in many ways didn't necessarily need to be influenza

specific, but could enhance many systems from the vaccine production architecture to our surveillance mechanisms.

SM: Now can you recall where you were and what you were doing when it became clear that this novel H1N1 virus was highly transmittable?

BG: I remember exactly where I was. It was a Saturday morning, and I was driving with my family to Baltimore to go to lacrosse camp. And I got a call from Nancy Cox at CDC to tell me about these cases that CDC had become aware of in Southern California, and then later in Texas. And the question was, there were two children in California who were detected as having this H1N1 virus, and the CDC had determined that it had some swine genetics to it. That was important because, while CDC sees these every once in while, I think there may be one or two a year like this, (most people have some exposure to pigs that accounts for how it is that people get infected with viruses like these, not always, but for the most part), here they had two kids in the same period of time who didn't know each other. And so while they were in the same general vicinity in California, it didn't appear that they had a common exposure.

That same phone call, she told me (Nancy is somebody who's in touch with everyone around the world in influenza, and they in touch with her) she was aware of some respiratory illnesses in Mexico and was trying to string those two together. So again, I remember exactly this conversation and how she was then going to be calling into Mexico to get a better sense of what they were seeing there.

SM: So at what point did you become involved in the response efforts?

BG: Well, I think that started it. It wasn't like that was the last call I had that day. I am sure there were, I can't remember exactly, but I know there were many other conversations about that ongoing investigation. And I forget exactly the timing of that one relative to when the cases...I think there were already those cases in Texas as well, at the same time, and that there were these two locations, and they didn't seem to have anything among the four of them in common that linked them together. And that plus this discussion that there was something going on in Mexico sort of strung them together in that, obviously, these were both along the U.S./Mexican border. And that

began the whole series. I can't think of a time when I then stepped away from it, because it went from these surveillance issues to immediately, into some of the vaccine issues, which is probably some of the stuff that I was more involved in. And knowing that as soon as they detect a virus like this, it's a new virus, that there is broad population immunity that is now transmitting among people - that's the kind of virus you worry about.

So, I immediately knew that Nancy and her team and others began thinking about how this virus could be turned into a vaccine. They go through a series of steps to do that, but that was the start of the clock of this - what's called a reference strain, or the seed virus that's then given to manufacturers - that ultimately was available to them about four or five weeks later.

SM: What were some of the major issues that you immediately had to contend with once it was recognized that this was something that was highly transmittable?

BG: Well, again, most of my sphere has to do with (at least from the National Vaccine Program office perspective,

and my day job is about the vaccine component of it,) making sure that that was on track. Again, that has it's own - once that gets started, it's got its own life, so to speak. So that was working, and there were other labs that were beginning to work on that. And essentially, that's the way the drill is supposed to work, that the labs who are charged as part of the WHO system on working on this began the process of developing these reference strains so the manufacturers could get to them. Obviously, that's where lots of people had lots of need for information.

Along the vaccine piece of it was how that part of the system was working from the laboratories to the manufacturers, beginning to think through with the manufacturers what this might mean for their manufacturing. And again, you'd probably want to talk to Robin Robinson at BARDA of how they were able to utilize their existing relationships with manufacturers and many of the existing contracts to begin to have the manufactures start making vaccine. Again, only on the vaccine part of it, at the end of April to early May was to make sure that they would begin the process of making a vaccine that was available for clinical trials, and the urgent need to get some of that information as soon as possible.

We had learned from the H5N1 virus that the vaccine against that virus was not terribly immunogenic. It required a very, very high dose: in two doses, even in healthy adults. At that point, with the H5 vaccine, essentially felt that we wouldn't be able to have a national, even a global, response without using an adjuvant that would enhance the immune response, and be able to allow more doses. So, that was in the back of our minds as this vaccine was being developed so that we had an early possible read on how immunogenic we thought the vaccine would be.

That was really on its own track as we began thinking about all the other components of this: from what this meant for border situations; what this meant for how antivirals would be used; how to communicate with the health care system and what they should be preparing for; how to better understand what was actually happening in Mexico, because at the beginning of it we are seeing the most severe disease and it was a very confusing time. I think people refer to it as 'the fog of war', until some of this stuff falls out and have a clear picture of what's actually happening on the ground.

That's relevant because in our thinking about pandemic preparedness, and particularly pandemic response, we had come up with something called the pandemic severity index, recognizing that not all pandemics are the same, and a response to a pandemic should be proportionate to the severity of it. And you'd be willing to do many more things to protect society against a severe pandemic with a high case fatality rate where you would have not only health disruptions, but, potentially, societal and economic disruptions. So, the severity index, which was developed by a broad interagency group over the preceding years, we're trying to use that as our barometer to figure out what the severity was, and therefore, what the level of response could be. I think it showed us that, again, in the fog of war, it's hard to sort that out. Because the data wasn't perfect, we had a lot more data about the number of people who were sick than the number of people who were infected. So, the numerator of those who were sick versus the denominator of those who may have been infected that may be asymptomatic or very sick, trying to figure out what that ratio would be. And I think, it taught us that it's not quite as nimble a tool as you may need, and that the response was developed without the ability to use the

severity index. And so, I think we've had that idea in place, but like many theories, when it comes to practice the data wasn't there to help us to allow us to use that.

SM: So how did you move forward once you realized that, what did you rely on?

BG: Well, I think that, again, this is where it's more of the tried and true methods of having teams go participate as part of a World Health Organization response. People from the CDC, and, I believe, from the Canadian government and maybe some other places, we're working with the Mexicans to try to get a better sense of what the magnitude of the problem actually was, to try to figure out how long it had been going on, and whether or not what we're seeing there was representative of something else.

Again, at the same time, we realized that many of the things of our earlier plans didn't quite fit what we were seeing. For a long time, because of the emergence of the H5 virus in Asia and many of the influenza viruses that seem to come from Asia, a lot of the thinking and modeling had assumed that these would emerge elsewhere, and that there would be therefore more time to put the pieces together

before it was transmitted broadly around the world. And essentially, by the time we saw what was happening we realized there were cases across the United States and beginning around the world. And I guess, in part, the fact that this occurred in a neighbor like Mexico with lots of travel in the United States back and forth to Mexico, and particularly with spring break and excess travel, showed how quickly these seeds from an outbreak in Mexico could find their way around the country.

SM: What were some of the underlying assumptions that guided your decision making process in the spring?

BG: Hmm. I think, as I said, we had to take a step back, because among our assumptions was that a virus would happen further away and there would be more time to be able to mount a response. And initially, some of the thinking was that if you could invest in containing an emerging outbreak elsewhere, that would buy you time for the response here. So, it was clear that that assumption wasn't gonna work in this case.

Other assumptions were that, there was broad population susceptibility at that point. I think that it wasn't clear

that there was some residual immunity in the elderly, again those kind of information were important to come forward.

There was a question of whether or not, because if this was an H1N1 virus, there would be any cross protection from the seasonal vaccine, and so there was a lot of work both at the CDC and elsewhere in animal studies and some human studies to better assess that. And just last week in the MMWR, there was another reassessment of that, because of the question of whether or not the existing seasonal vaccine would buy you any protection, and it didn't. So, I think that the question was how best to control an outbreak at the time that you are developing a vaccine which would be the most important tool, and knowing that it would take some time for a vaccine to be developed.

I think that maybe among the things we might, in hindsight, have thought differently about are some of the words we've used, because I think that that's influenced a lot of the perspective about how this outbreak is going on. I think the idea that this was a 'mild' outbreak was never quite the right word. Just in the past few days CDC has readjusted the way it's doing its counting, and it's increased the number of - based on extrapolations not just

laboratory testing - people who have been hospitalized, the number of fatalities that have been caused by this virus over time. It's not meant to - it makes this a more severe virus - but it makes it more clear what the magnitude of the problem actually is.

So, I think we've had a hard time explaining to people how this is different than seasonal flu. And seasonal flu, most of the problems are in the elderly; that's where the majority of the fatalities are. In this one, most of the problem is in the younger people, and I think that that's been hard for us to communicate.

I think another word that has been a complicated one is 'new', is 'novel', and while there's no question that it's a novel virus, I think that to a lot of people that word novel means a lot of different things. And it's transposed into many, by thinking if this is a novel virus then what we're making is a novel vaccine. And what we see around the country now, at least in some of the polls we're seeing, is that there's a split between those who are desperate to trying to find a vaccine for themselves and their family, and almost the other half of the country who thinks that

this is way overblown, that the disease is minimal and the vaccine is dangerous.

Again, we've been trying to explain to people why we have the comfort that we do in this vaccine. It's made exactly the way the seasonal vaccine is made, by all the same people with all the same process and all the same tests. It took the same amount of time, but nevertheless, the country seems to be split on that. And there are people who are very cautious and feel that the risks are much too high, and then again, there are people who are very concerned about the disease and its implications, and are trying to find what they can do to protect themselves and their children. So, I think that the novel word is one that is unfortunate in that while it was descriptive at the time it burned us as far as how that would transpose onto the vaccine. I don't know what we're going to do over time as this persists beyond December 31st, when this is no longer the novel 2009 H1N1. We'll have to see in hindsight how that gets handled.

The other word, I think, is the 'swine' word. And while, maybe, in other places there's a lot that's associated with swine from the perspective of vaccines, to many it's a

flashback to 1976 when we had the swine flu experience; a time when there was concern about the emergence of a new virus that showed itself to have some fatality and some ability to transmit among people. A vaccine program was developed, the vaccine developed, and a program ensued. The disease never showed up, in contrast to now where there's plenty of disease around and people are very concerned about what this disease might mean, and particularly what is in the future. In 1976, the vaccine, a vaccination program was mounted trying to anticipate an outbreak that never came. So, in that situation, the benefit to risk ratio, the risk of a vaccine ended up being higher than the benefit of the vaccine, since the disease didn't occur. So, again, the swine word was part of it as well.

I think the pandemic word has also been confusing. While its definition is geographic across the world, I think that as we've gone to the numbering system the WHO uses from Phases 3, 4, 5 and 6, and particularly in the spring when the Director General of the World Health Organization was escalating this, it had much more of a visceral tie to it than I think anybody had anticipated. I remember when I was taking my son, who is in 6th grade, to school and we heard Margaret Chan who is the director general of the World

Health Organization on the radio saying, "Now, we're at level 5, and a global pandemic is imminent." So, to an eleven year old, that's a pretty powerful phrase, and he just said, "Well, if a pandemic is imminent do I have to do my homework?". So, I think that there is, again, I think that we didn't fully understand that because if the weather forecaster tells you that it's gone from a tropical storm to a hurricane, to, I don't know, a level 5 hurricane, it means very different things. And I think that that's confused people, because for years they saw these endless pictures of 1918 and body bags from the 1918 epidemic, and now we have a global pandemic that was 'mild'. And I think that people have a hard time putting those together. So, in sum, we have a series of words; I don't think they all align perfectly. And then that leads people to be very confused about what it all means, and what it means for them, and at the same time, what the government is doing about all this.

SM: So, essentially, once you got a better understanding of what was happening in terms of the intensity and the degree of transmission from person to person, your assumptions changed by the fall?

BG: Well, I think a couple of things. (And I'll have to break shortly and we can pick up again.) I think that in the spring, we were all surprised that a virus like this would show up when it did. The assumption is that these viruses are in the cold and flu season, this one showed up late in the spring and it persisted. The idea that there was these waves that come and go, I think that that was also not entirely true. While there was a lot less transmission over the summer, it persisted, and I think it has lots to do, not so much with changes in the climate and its effect on the virus, but changes in society and social mixing patterns, because we continue to see outbreaks in summer camps and in recruit camps from the military and the like, but much lower. But it never went away, and you just don't see that. And so I think there's some huge contrast between the way this virus behaves and the way that seasonal viruses normally behave.

We then shifted a lot of our focus on two things simultaneously about enhancing our preparedness for a "fall wave" with the anticipation that when society resumed its normal patterns - people went back to school, and we got into the cold and flu season - that we're likely to see an

uptick. At the same time, we spent a lot of effort working with and understanding what was going on in the Southern Hemisphere to see how this virus worked its way there, and what patterns were developing there to see whether it was similar to what we had seen in the spring in the Northern Hemisphere or different, and also might be a predictor for what might happen in the fall.

So I'll cut there, and we'll resume. This was good.

End of Interview

Broad Themes

- History of National Vaccine Program Office
    - National Vaccine Injury Compensation Program
    - Draft Pandemic Preparation Plan, 2004
    - HHS Pandemic Preparation Plan, 2005
    - National Strategy for Pandemic Infrastructure Preparedness
    - White House Plan: $7.1 Billion budget
- H5N1 Virus
- 1918 epidemic
- Non-influenza response infrastructure investment
- Reference strain
- Vaccine production process – response effort
- H5 and immunogenicity of H1N1
- Pandemic Severity Index
- WHO collaborative response – CDC, Mexico, Canada
- Assumptions of pandemic planning response
    - Asian origins versus America
    - H5 strain versus H1
    - Broad population susceptibility and elderly immunity
    - Cross protection from seasonal vaccine
    - Time frame for vaccine development

- Winter seasonal flu versus H1N1 perennial pattern

- Language of H1 Response – problems with
  - 'Mild'
  - 'New' or 'Novel' virus
  - 'Swine' origin
  - 'Pandemic' and 1918 comparison

Follow Up

Names:

Documents: